EDITORIAL ARTICLES.

GRASER ON THE ADHESIONS OF SEROUS MEMBRANES.[1]

THE question of the processes in the healing of wounds will always be of interest to the surgeon. Every improvement in the histological technique in this line has been of great advantage; old ideas have been confirmed and new ones established. In recent times, new methods have been invented which have contributed very greatly towards advancing our knowledge of the living cell. Such methods have enabled us to follow the changes in growing cells by fixing the cells at any stage of their development for microscopical study. A key to the progress of development in the individual cell is found in the mitoses which can be fixed at any stage. The vital energy of the cell can be discovered by other means which show defects in its vitality, as the appearance of free fragments of nuclei within the cell, the changes in the staining capacity of the cell, manifested sometimes by an inability to take stains and sometimes by the appearance of diffuse staining.

One of the greatest advances made in this line was the fibrin stain invented by Weigert.[2] This consists in a staining with aniline-water-gentian-violet, and a subsequent decolorization of the stain, after fixing with iodine, with aniline oil, and xylol. By this method the tissues give up their color, while the fibrin remains an intense blue.

Another advantage of the method is that most of the micro-organisms which are present also remain stained. This must be regarded as a sort of micro-chemical reaction.

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[1] Verhandlungen der deutschen Gesellschaft für Chirurgie, XXIV Kongress, 1895.

[2] Fortschritte der Medicin, 1887, No. 8.

The material which first causes adhesion in wounds, and which was designated by Hunter by the term "gluten," and which, in more recent times, has been studied by Thiersch, Wywodzoff, Gussenbauer, and others, has been demonstrated by the method of staining conceived by Weigert to be fibrin deposited from the plasma of the blood.

The origin of this fibrin in the living body in inflammations and also in the dead state—*i.e.*, the coagulation of drawn blood—has been much discussed and disputed. The demonstrations made by Alexander Smith concerning the importance of certain fibrinogenous substances have been of great importance. He showed that there was constantly dissolved in the plasma of the blood a certain substance or substances which could be converted into fibrin by the action of a ferment which was liberated by the disintegration of the cellular elements.

By investigating this fibrin-formation and studying its *rôle* in the adhesion of wounds and serous surfaces in animal experiments, one observes the delicate fibrinous net-work which penetrates everywhere in the field of study and includes a variety of cells, some of which are in good condition and some in a state of inanition.

In a large number of observations, Graser found that fibrin was always formed between the edges of wounds and between adherent serous surfaces, and that this formation was greater in proportion to the increased degree of inflammation due to chemical or mechanical irritation, but that where suppuration occurred there was no fibrin formed either in the presence of pus or in its immediate vicinity.

The following experiment was made upon a dog: After opening the abdomen in the linea alba, the two halves of the abdominal wall were drawn up into a ridge so that the two peritoneal surfaces were opposed, and by the use of lead plates were held in this relation with sutures. After forty-eight hours there was an adherence of the peritoneal surfaces in many places. At other places the surfaces lay very loosely together, so that very gentle traction sufficed to separate them. Microscopical examination showed that at the places where there were firm adhesions there was a rich deposit of fibrin in the form of fibres and clumps, including many cells in their meshes. At the edge of this firmly adherent portion, at which the peritoneum was not adherent but formed a very small intermediary space, could be seen structures which gave an answer to the much mooted question. Not far from a place where the adhesions were firm was a small, free space between the two peritoneal surfaces. Here the endothelium of the peritoneum presented a very delicate border composed of nothing but delicate fibres studded with nuclear enlargements, the underlying endothelial cells being swollen.

In other places altered endothelial cells were found but rarely. Here and there were found holes where one or more endothelial cells were absent and which were filled with fibrin. Near such places were found others where there were no well-preserved endothelial cells, and where many of the cells appeared simply as swollen, unstained masses with scarcely discernible nuclei. These masses were dislodged from their normal ground and appeared in the space between the two layers of peritoneum.

Out of the large number of sections examined microscopically there was one class of especial interest, in which the endothelium was almost entirely gone and the ground membrane was covered with a layer of fibrin. In the middle, between the opposed peritôneal surfaces, was an amorphous deposit due to the coagulation of the albuminous inflammatory plasma by the process of hardening and fixing the specimen. It might be supposed that this plasma, which is so rich in fibrinogen, is the source of the fibrinous deposits. This has been found not to be the case.

The middle portion remained free, the fibrin fibrillæ radiating from the peritoneum inward towards the centre. At this place an active inflammation was not evidenced by an accumulation of leucocytes. Extravasated leucocytes were not present at all, or only in very small numbers. Nor were bacteria to be found anywhere in the field. The tissue was, however, œdematous, and the individual cells somewhat swollen and separated from one another by the serous transudate. The endothelium was undoubtedly damaged by interference with its nourishment, and presented marked differences from the normal tissue. This damage to the endothelium was not so pronounced as to be irreparable.

In the surrounding tissue a considerable amount of fibrin was found in the meshes of the connective tissue. In some places could be seen degenerating connective-tissue cells, surrounded by a thick layer of fibrin from which a delicate fibrinous net-work radiated out on all sides.

Before the peritoneal endothelium became firmly adherent it was found to undergo regressive changes. With the progress of these changes a deposit of fibrin takes place about these cells. When such fibrin net-work from the two sides comes together, adhesion takes place, while the cells which originally covered the surfaces continue in their process of degeneration.

Graser has already demonstrated that the interposed peritoneal endothelium perishes almost entirely with the adhesion of the two surfaces.

Judging from these researches, the thought occurs that the perishing endothelial cells have something to do with the formation of the fibrin. This must be conceded, but the fibrin itself is deposited out of the blood-plasma, the breaking-down cells furnish something which is, however, essential to the depositing of the fibrin out of the fluid plasma.

The investigations of Alexander Smith and his pupils showed that the breaking-down leucocytes were the source of this fibrinogen.

Loewit[1] examined the blood in the vessels, and observed an escape and separation of material from the protoplasm of the cell-body of the white blood-corpuscles in the form of fibres and granules. This he called plasmoschisis.

Lilienfeldt,[2] in an elaborate essay, observed that a substance contained in the cell-nuclei, called leuconuclein, possessed in a high degree the power of causing coagulation and the formation of fibrin. By histological experiment he demonstrated that fibres of fibrin were attached to the nuclei of leucocytes; that thereby the leucocytes tended to adhere to the vessel walls, and that certain nuclear ingredients in some manner extracted from the fibrin threads passed out of the cell-body.

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[1] Zeigler's Beiträge zür pathologische Anatomie, 1889, v, p. 471.

[2] Zeitschrift für pathologische Chemie, 1894, Bd. xx, p. 89.

Gradually the nucleus loses in a great degree its power of taking staining reagents. Lilienfeldt found that this power depended upon the presence of the nuclein substance above mentioned. Thus, when the nuclei give up their nuclein to the plasma to form fibrin they lose the power of taking stains. This phenomenon of the transit of the nuclein has been designated as karyoschisis.

Notwithstanding the apparent differences, it is well to consider the plasmoschisis of Loewit and the karyoschisis of Lilienfeldt under the same head.

Hauser[1] found, with the aid of Weigert's stain, that in the inflammatory deposits of fibrin an especially large amount of fibrin accumulated about the degenerated cells, and he called this place the "coagulation centre."

He found in the inflamed and œdematous connective tissue in the vicinity of a laryngeal diphtheria a fine-meshed fibrin net-work, in which were numerous nodular points, which looked like particles of dirt in the specimen. By the use of a stronger lens, however, it could be plainly seen that each of these blue-stained points was a collection of fibrin enclosing in its midst a connective-tissue cell or a colorless blood-corpuscle, and sending out in all directions radii of fine fibrin fibres. The cell included in the centre showed the characteristic changes of a dying cell. These pictures were clearest in those specimens in which the amount of fibrin was the least.

These experiments and observations teach that this adhesion cannot take place without the degeneration of cells. These experiments show that two peritoneal surfaces sewed together for a large area can lie together for days without reaction. This may be the case with loops of intestine sutured together, adhesion taking place only at the places of the passage of sutures. Between these places, if no damage has been done to the peritoneum, no adhesion takes place.

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[1] Deutsche Archiv für klinische Medicin, Bd. L, p. 363.

A practical application of these principles can be made use of in operations in the abdomen, in which it is desirable to diminish as much as possible the formation of adhesions. As a result of a series of experiments, it was found that all antiseptics, especially sublimate of mercury and carbolic, damage to a great degree the endothelium of the peritoneum; that thymol and boric acid do this damage in a much lesser degree than the others, and that even the dry handling of the peritoneum has a damaging effect. If the exposed peritoneum is covered with a layer of absorbent gauze so that evaporation is not prevented, and left for half an hour, there will appear upon the intestinal as well as parietal peritoneum, as a result of the disturbance in the superficial cells, a deposit of fibrin over the exposed surface. On the other hand, the cells remain unchanged if the peritoneum is kept moistened with warm salt solution.

These experiments are of practical importance, as are those of Walthard[1] upon the drying influence of the air upon the peritoneum.

Associated with its easy vulnerability the peritoneum is characterized by a great capacity for regeneration. In order for adhesions to take place, it is necessary that two damaged surfaces shall be in undisturbed contact for a considerable length of time. Some irritation of the vessels with escape of plasma into the tissues is also necessary.

Walthard showed that the action of dry air upon the peritoneum for twenty minutes, with infection, caused severe damage to the endothelial cells, and resulted in the formation of adhesions or in inflammatory thickening.

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[1] Korrespondenzblatt für schweizer Aerzte, 1893.